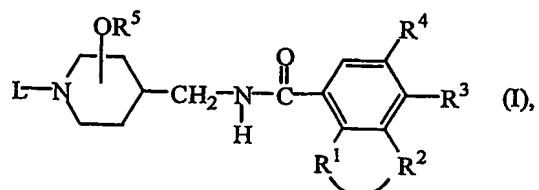


Claims

1. A compound of formula (I)



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a stereochemically isomeric form thereof, an *N*-oxide form thereof, or a pharmaceutically acceptable acid or base addition salt thereof, wherein -R¹-R²- is a bivalent radical of formula

10	-O-CH ₂ -O-	(a-1),
	-O-CH ₂ -CH ₂ -	(a-2),
	-O-CH ₂ -CH ₂ -O-	(a-3),
	-O-CH ₂ -CH ₂ -CH ₂ -	(a-4),
	-O-CH ₂ -CH ₂ -CH ₂ -O-	(a-5),
15	-O-CH ₂ -CH ₂ -CH ₂ -CH ₂ -	(a-6),
	-O-CH ₂ -CH ₂ -CH ₂ -CH ₂ -O-	(a-7),
	-O-CH ₂ -CH ₂ -CH ₂ -CH ₂ -CH ₂ -	(a-8),

wherein in said bivalent radicals optionally one or two hydrogen atoms on the same or a different carbon atom may be replaced by C₁-alkyl or hydroxy.

20 R^3 is C_{1-6} alkyl, C_1-C_6 alkyloxy or halo;

R^4 is hydrogen or halo:

provided that when R^3 and R^4 are both halo, then the bivalent radical- R^1-R^2- is of formula (a-5):

25 R⁵ is hydrogen or C₁-6alkyl, and the -OR⁵ radical is situated at the 3- or 4-position of the piperidine moiety;

L is hydrogen, or L is a radical of formula

-Alk-R⁶ (b-1)

-Alk-X-R⁷ (b-2)

-Alk-Y-C(=O)-R⁹

30 -Alk-Z-C(=O)-NR¹¹R¹² (b-4),

wherein each Alk is C₁₋₁₂alkanediyl; and

R⁶ is hydrogen; hydroxy; cyano; C₃₋₆cycloalkyl; C₁₋₆alkylsulfonylamino; aryl or Het:

R⁷ is C₁₋₆alkyl; C₁₋₆alkyl substituted with hydroxy; C₃₋₆cycloalkyl; aryl or Het:

X is O, S, SO₂ or NR⁸; said R⁸ being hydrogen or C₁₋₆alkyl;
 R⁹ is hydrogen, C₁₋₆alkyl, C₃₋₆cycloalkyl, hydroxy or aryl;
 Y is a direct bond, or NR¹⁰ wherein R¹⁰ is hydrogen or C₁₋₆alkyl;
 Z is a direct bond, O, S, or NR¹⁰ wherein R¹⁰ is hydrogen or C₁₋₆alkyl;
 5 R¹¹ and R¹² each independently are hydrogen, C₁₋₆alkyl, C₃₋₆cycloalkyl, or R¹¹ and R¹² combined with the nitrogen atom bearing R¹¹ and R¹² may form a pyrrolidinyl, piperidinyl, piperazinyl or 4-morpholinyl ring both being optionally substituted with C₁₋₆alkyl;
 aryl represents unsubstituted phenyl or phenyl substituted with 1, 2 or 3 substituents
 10 each independently selected from halo, hydroxy, C₁₋₆alkyl, C₁₋₆alkyloxy, C₁₋₆alkylcarbonyl, nitro, trifluoromethyl, amino, aminocarbonyl, and aminosulfonyl; and
 Het is furanyl; furanyl substituted with C₁₋₆alkyl or halo;
 15 tetrahydrofuranyl; tetrahydrofuranyl substituted with C₁₋₆alkyl;
 dioxolanyl; dioxolanyl substituted with C₁₋₆alkyl;
 dioxanyl; dioxanyl substituted with C₁₋₆alkyl;
 tetrahydropyranyl; tetrahydropyranyl substituted with C₁₋₆alkyl;
 20 2,3-dihydro-2-oxo-1H-imidazolyl; 2,3-dihydro-2-oxo-1H-imidazolyl substituted with one or two substituents each independently selected from halo, or C₁₋₆alkyl;
 pyrrolidinyl; pyrrolidinyl substituted with one or two substituents each independently selected from halo, hydroxy, or C₁₋₆alkyl;
 25 pyridinyl; pyridinyl substituted with one or two substituents each independently selected from halo, hydroxy, C₁₋₆alkyl;
 pyrimidinyl; pyrimidinyl substituted with one or two substituents each independently selected from halo, hydroxy, or C₁₋₆alkyl;
 pyridazinyl; pyridazinyl substituted with one or two substituents each independently selected from hydroxy, C₁₋₆alkyloxy, C₁₋₆alkyl or halo;
 30 pyrazinyl; pyrazinyl substituted with one or two substituents each independently selected from hydroxy, C₁₋₆alkyloxy, C₁₋₆alkyl or halo.

2. A compound as claimed in claim 1 wherein the -OR⁵ radical is situated at the 3-position of the piperidine moiety having the trans configuration.

35 3. A compound as claimed in claim 2 wherein the absolute configuration of said piperidine moiety is (3S, 4S).

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4. A compound as claimed in any of claims 1 to 3 wherein -R¹-R²- is a radical of formula (a-5), R³ is chloro and R⁴ is chloro.

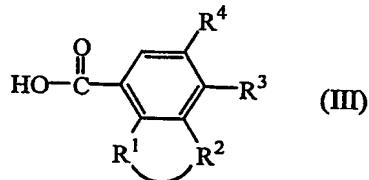
5. A compound as claimed in any of claims 1 to 3 wherein -R¹-R²- is a radical of formula (a-5), R³ is chloro and R⁴ is bromo.

6. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a therapeutically active amount of a compound according to any of claims 1 to 5.

10 7. A process for preparing a pharmaceutical composition according to claim 6 wherein a therapeutically active amount of a compound according to any of claims 1 to 5 is intimately mixed with a pharmaceutically acceptable carrier.

15 8. A compound according to any of claims 1 to 5 for use as a medicine.

9. A compound of formula (III).



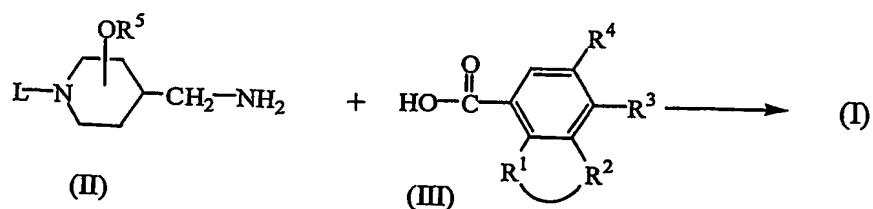
wherein

20 -R¹-R²- is a bivalent radical of formula

$$-\text{O}-\text{CH}_2-\text{CH}_2-\text{CH}_2-\text{O}- \quad (\text{a-5}),$$
 wherein in said bivalent radicals optionally one or two hydrogen atoms on the same or a different carbon atom may be replaced by C₁₋₆alkyl or hydroxy;
 R³ is C₁₋₆alkyl, C₁₋₆alkyloxy, or halo; and
 R⁴ is hydrogen or halo.

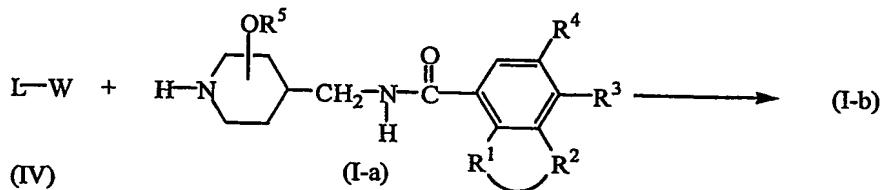
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10. A process for preparing a compound of formula (I) wherein
 a) an intermediate of formula (II) is reacted with an carboxylic acid derivative of formula (III) or a reactive functional derivative thereof;

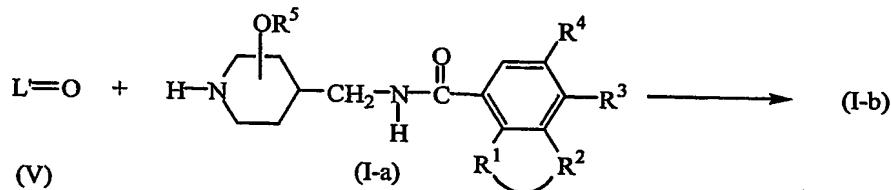


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b) an intermediate of formula (IV) is *N*-alkylated with a compound of formula (I-a), defined as a compound of formula (I) wherein L represents hydrogen, in a reaction-inert solvent and, optionally in the presence of a suitable base, thereby yielding compounds of formula (I-b), defined as compounds of formula (I) wherein L is other than hydrogen;



10 c) an appropriate ketone or aldehyde intermediate of formula $L'=O$ (V), said $L'=O$ being a compound of formula $L-H$, wherein two geminal hydrogen atoms in the C_{1-12} alkanediyl moiety are replaced by $=O$, is reacted with a compound of formula (I-a), thereby yielding compounds of formula (I-b);



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wherein in the above reaction schemes the radicals $-R^1-R^2-$, R^3 , R^4 and R^5 are as defined in claim 1 and W is an appropriate leaving group;

20 d) or, compounds of formula (I) are converted into each other following art-known transformation reactions; or if desired; a compound of formula (I) is converted into a pharmaceutically acceptable acid addition salt, or conversely, an acid addition salt of a compound of formula (I) is converted into a free base form with alkali; and, if desired, preparing stereochemically isomeric forms thereof.

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